Patent
259/181

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	**Continuation 1.53(b)**
Alison, et al.,	**Serial No. 09/256,630**
Serial No.: Not Yet Assigned	**Group Art Unit: 1632**
Filed: Herewith	**Examiner:**
For: COMBINATIONS AND METHODS FOR PROMOTING IN VIVO LIVER CELL PROLIFERATION AND ENHANCING IN VIVO LIVER-DIRECTED GENE TRANSDUCTION	

PRELIMINARY AMENDMENT FOR CONTINUATION APPLICATION

BOX **PATENT APPLICATION**
Commissioner for Patents
Washington, D.C. 20231

Sir:

Before examining this Continuation Application based on application Serial No. 09/256,630, kindly amend this Continuation Application as follows:

In the Specification:

Please amend the specification as follows:

At page 1, after the title insert:

--This application is a Continuation of Serial No. 09/256,630, filed on February 23, 1999.--

At page 2, line 15, change "receptor based" to --receptor-based--.

At page 2, line 22, change "liver directed" to --liver-directed--.

At page 14, line 12, change "liver directed" to --liver-directed--.

At page 14, line 14, change "liver directed" to --liver-directed--.

At page 15, line 16, delete "the".

At page 22, line 8, change "quite" to -- quiet –

At page 23, line 12, change "respose" to -- response --.

At page 26, line 22, change "or" to -- of --.

At page 28, line 16, change "poly-adenilation" to --poly-adenylation--.

In the Claims:

Please add the following new claims:

26. A method for improving the efficiency of *in vivo* liver cell retroviral transduction, the method comprising, inducing a semi-synchronous wave of *in vivo* liver cell proliferation by concurrently administering a composition comprising tri-iodothyronine (T3) and keratinocyte growth factor (KGF), and further comprising administering to the liver a retroviral vector complexed with cationic liposomes subsequent to the induction of liver cell proliferation, thereby increasing transduction efficiency.

27. The method of claim 26, the cationic liposome comprising DiOctadecylamidoGlycylSpermine (DOGS).

28. A method of treatment comprising:

inducing a semi-synchronous wave of liver cell proliferation by concurrently contacting the liver cells with a composition comprising tri-iodothyronine (T3) and keratinocyte growth factor (KGF);

contacting the liver cells with a retroviral vector containing a nucleic acid that encodes the RNA, protein or polypeptide to be expressed;

and expressing the RNA, protein or polypeptide.

29. The method of claim 28, further comprising inducing the liver cell proliferation in vitro.

30. The method of claim 28, further comprising inducing the liver cell proliferation in vivo.

31. The method of claim 28, wherein the RNA comprises ribozymes.

32. The method of claim 28, wherein said RNA comprises anti-sense RNA.

33. The method of claim 28, wherein the nucleic acid comprises DNA.

34. The method of claim 28, wherein the nucleic acid comprises RNA.

35. A method of treatment comprising,

the administration of a composition comprising an effective amount of tri-iodothyronine (T3) and an effective amount of keratinocyte growth factor (KGF) , wherein the composition is in an effective amount that induces a semi-synchronous wave of liver cell proliferation upon administration *in vivo* in a subject;

and further comprising administering to the liver, subsequent to the liver cell proliferation, a retroviral vector containing a the nucleic acid that encodes the RNA, protein or polypeptide to be expressed;

expressing the RNA, protein or polypeptide, thereby treating the condition.

36. The method of claim 35 wherein the effective amount of T3 is ranging from about 400 μg per kg of body weight of the subject to about 40 mg per kg of body weight of the subject.

37. The method of claim 36, wherein the effective amount of T3 is about 4 mg per kg of body weight of the subject.

38. The method of claim 35, wherein the effective amount of KGF is ranging from about 100 μg per kg of body weight of the subject to about 10 mg per kg of body weight of the subject.

39. The method of claim 38, wherein the effective amount of KGF is about 1 mg per kg of body weight of the subject.

40. The method of claim 35, wherein the effective amount of T3 and the effective amount of KGF is in a ratio of about 4:1 by weight.

41. The method of claim 40, wherein the effective amount of T3 is in a dose of about 4 mg per kg of body weight of the subject and the effective amount of KGF is in a dose of about 1 mg per kg of body weight of the subject.

42. The method of claim 41, wherein the composition is administered subcutaneously.

43. The method of claim 41, wherein the composition is administered intravenously.

44. The method of claim 41, wherein the composition is administered intramuscularly.

45. The method of claim 41, wherein the composition is administered intraperitoneally.

46. The method of claim 41, wherein the composition is administered directly into the liver.

47. The method of claim 35, the retroviral vector further comprising a cationic liposome.

48. The method of claim 47, the cationic liposome comprising DiOctadecylamidoGlycylSpermine (DOGS).

49. The method of claim 35 wherein the retroviral vector is administered between about 6 hours and 14 days after administration of the pharmaceutical composition.

50. The method of claim 35 wherein the retroviral vector is administered between about 24 hours and 8 days after administration of the pharmaceutical composition.

51. A method for treating or preventing cirrhosis of the liver comprising concurrently administering to a subject a composition comprising an effective amount of T3 and an effective amount of KGF, thereby inducing a semi-synchronous wave of liver cell proliferation *in vivo*.

REMARKS

This application is a Continuation Application of Serial No. 09/256,630, filed February 23, 1999 in which the pending claims are believed to be allowable. New claims 26 - 51 have been added by this Preliminary Amendment to claim the invention in a different manner and scope than any of the allowable pending claims of the parent application.

A favorable consideration of claims 26 - 51 is respectfully requested.

Respectfully submitted,

LYON & LYON LLP

Dated: January 24, 2001

By: _____
Michael J. Wise
Reg. No. 34,047

633 West Fifth Street, Suite 4700
Los Angeles, California 90071-2066
(213) 489-1600